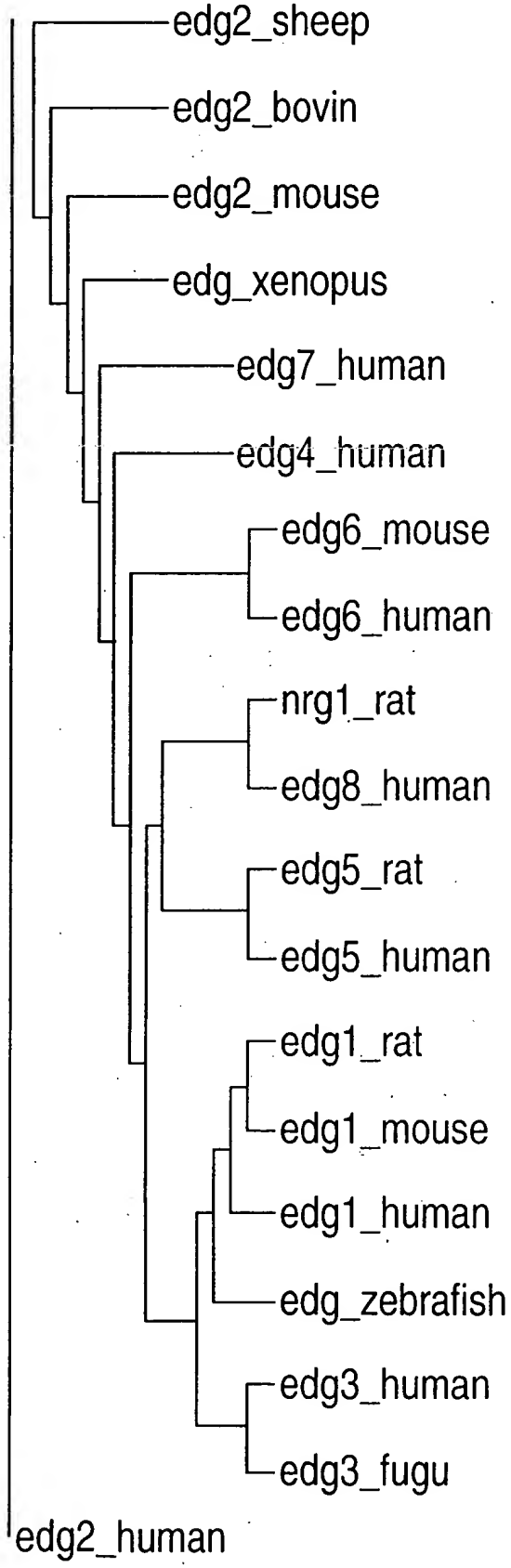
# FIG. 1A-1

```
1 ATGGAGTCGGGGCTGCTGCGGCCGGCGCCGGTGAGCGAGGTCATCGTCCTGCATTACAAC
  M  E  S  G  L  L  R  P  A  P  V  S  E  V  I  V  L  H  Y  N

61 TACACCGGCAAGCTCCGCGGTGCGCGCTACCAGCCGGGTGCCGGCCTGCGCGCCGACGCC
   Y  T  G  K  L  R  G  A  R  Y  Q  P  G  A  G  L  R  A  D  A

121 GTGGTGTGCCTGGCGGTGTGCGCCTTCATCGTGCTAGAGAATCTAGCCGTGTTGTTGGTG
    V  V  C  L  A  V  C  A  F  I  V  L  E  N  L  A  V  L  L  V

181 CTCGGACGCCACCCGCGCTTCCACGCTCCCATGTTCCTGCTCCTGGGCAGCCTCACGTTG
    L  G  R  H  P  R  F  H  A  P  M  F  L  L  L  G  S  L  T  L

241 TCGGATCTGCTGGCAGGCGCCGCCTACGCCGCCAACATCCTACTGTCGGGGCCGCTCACG
    S  D  L  L  A  G  A  A  Y  A  A  N  I  L  L  S  G  P  L  T

301 CTGAAACTGTCCCCCGCGCTCTGGTTCGCACGGGAGGGAGGCGTCTTCGTGGCACTCACT
    L  K  L  S  P  A  L  W  F  A  R  E  G  G  V  F  V  A  L  T

361 GCGTCCGTGCTGAGCCTCCTGGCCATCGCGCTGGAGCGCAGCCTCACCATGGCGCGCAGG
    A  S  V  L  S  L  L  A  I  A  L  E  R  S  L  T  M  A  R  R

421 GGGCCCGCGCCCGTCTCCAGTCGGGGGCGCACGCTGGCGATGGCAGCCGCGGCCTGGGGC
    G  P  A  P  V  S  S  R  G  R  T  L  A  M  A  A  A  A  W  G

481 GTGTCGCTGCTCCTCGGGCTCCTGCCAGCGCTGGGCTGGAATTGCCTGGGTCGCCTGGAC
    V  S  L  L  L  G  L  L  P  A  L  G  W  N  C  L  G  R  L  D

541 GCTTGCTCCACTGTCTTGCCGCTCTACGCCAAGGCCTACGTGCTCTTCTGCGTGCTCGCC
    A  C  S  T  V  L  P  L  Y  A  K  A  Y  V  L  F  C  V  L  A
```

# FIG. 1A-2

```
601 TTCGTGGGCATCCTGGCCGCTATCTGTGCACTCTACGCGCGCATCTACTGCCAGGTACGC
    F  V  G  I  L  A  A  I  C  A  L  Y  A  R  I  Y  C  Q  V  R

661 GCCAACGCGCGGCGCCTGCCGGCACGGCCCGGGACTGCGGGGACCACCTCGACCCGGGCG
    A  N  A  R  R  L  P  A  R  P  G  T  A  G  T  T  S  T  R  A

721 CGTCGCAAGCCGCGCTCGCTGGCCTTGCTGCGCACGCTCAGCGTGGTGCTCCTGGCCTTT
    R  R  K  P  R  S  L  A  L  L  R  T  L  S  V  V  L  L  A  F

781 GTGGCATGTTGGGGCCCCCTCTTCCTGCTGCTGTTGCTCGACGTGGCGTGCCCGGCGCGC
    V  A  C  W  G  P  L  F  L  L  L  L  L  D  V  A  C  P  A  R

841 ACCTGTCCTGTACTCCTGCAGGCCGATCCCTTCCTGGGACTGGCCATGGCCAACTCACTT
    T  C  P  V  L  L  Q  A  D  P  F  L  G  L  A  M  A  N  S  L

901 CTGAACCCCATCATCTACACGCTCACCAACCGCGACCTGCGCCACGCGCTCCTGCGCCTG
    L  N  P  I  I  Y  T  L  T  N  R  D  L  R  H  A  L  L  R  L

961 GTCTGCTGCGGACGCCACTCCTGCGGCAGAGACCCGAGTGGCTCCCAGCAGTCGGCGAGC
    V  C  C  G  R  H  S  C  G  R  D  P  S  G  S  Q  Q  S  A  S

1021 GCGGCTGAGGCTTCCGGGGGCCTGCGCCGCTGCCTGCCCCCGGGCCTTGATGGGAGCTTC
     A  A  E  A  S  G  G  L  R  R  C  L  P  P  G  L  D  G  S  F

1081 AGCGGCTCGGAGCGCTCATCGCCCCAGCGCGACGGGCTGGACACCAGCGGCTCCACAGGC
     S  G  S  E  R  S  S  P  Q  R  D  G  L  D  T  S  G  S  T  G
1141 AGCCCCCGGTGCACCCACAGCCGCCCGGACTCTGGTATCAGAACCGGCTGCAGACTGA
     S  P  G  A  P  T  A  A  R  T  L  V  S  E  P  A  A  D  *
```

# FIG. 1B



# FIG. 1C-1

```
                1                                                      60
edg2_human  MAAISTSIPV ISQPQETAMN EPQCFYNESI AFFYNRSGKH LAT.EWNTVS KLVMGL..GI
edg7_human  ---------- --------MN E..CHYDKHM DFFYNRSNTD TVD.DW.TGT KLVIVLCVGT
edg4_human  ---------- -------MVI MGQCYYNETI GFFYNNSGKE LSS.HWR..P KDVVVVALGL
edg1_human  -----MGPTS VPLVKAHRSS VSDYVNYDII VRHYNYTGKL ..NISADKEN SIKLTSVVFI
edg3_human  ---------- --MATALPPR LQPVRGNETL REHYQYVGKL AGRLKEASEG S.TLTTVLFL
edg5_human  ---------- ------MGSL YSEYLNPNKV QEHYNYTKE. ..TLETQETT SRQVASAFIV
edg8_human  ---------- -----MESGL LRPAPVSEVI VLHYNYTGKL RG.ARYQPGA GLRADAVVCL
edg6_human  -----MNATG TPVAPESCQQ LAAGGHSRLI VLHYNHSGRL AGR.GGPEDG GLGALRGLSV

                61                                                     120
edg2_human  TVCIFIMLAN LLVMVAIYVN RRFHFPIYYL MANLAAADFF AGLAYFYLMF MTGPNTRRLT
edg7_human  FFCLFIFFSN SLVIAAVIKN RKFHFPFYYL LANLAAADFF AGIAYVFLMF NTGPVSKTLT
edg4_human  TVSVLVLLTN LLVIAAIASN RRFHQPIYYL LGNLAAADLF AGVAYLFLMF HTGPRTARLS
edg1_human  LICCFIILEN IFVLLTIWKT KKFHPPMYYF IGNLALSDLL AGVAYTANLL LSGATTYKLT
edg3_human  VICSFIVLEN LMVLIAIWKN NKFHNRMYFF IGNLALCDLL AGIAYKVNIL MSGKKTFSLS
edg5_human  ILCCAIVVEN LLVLIAVARN SKFHSAMYLF LGNLAASDLL AGVAFVANTL LSGSVTLRLT
edg8_human  AVCAFIVLEN LAVLLVLGRH PRFHAPMFLL LGSLTLSDLL AGAAYAANIL LSGPLTLKLS
edg6_human  AASCLVVLEN LLVLAAITSH MRSRRWVYYC LVNITLSDLL TGAAYLANVL LSGARTFRLA

                121                                                    180
edg2_human  VSTWLLRQGL IDTSLTASVA NLLAIAIERH ITVFR.MQLH TRMSNRRVVV VIVVIWTMAI
edg7_human  VNRWFLRQGL LDSSLTASLT NLLVIAVERH MSIMR.MRVH SNLTKKRVTL LILLVWAIAI
edg4_human  LEGWFLRQGL LDTSLTASVA TLLAIAVERH RSVMA.VQLH SRLPRGRVVM LIVGVWVAAI
edg1_human  PAQWFLREGS MFVALSASVF SLLAIAIERY ITMLK.MKLH NGSNNFRLFL LISACWVISL
edg3_human  PTVWFLREGS MFVALGASTC SLLAIAIERH LTMIK.MRPY DANKRHRVFL LIGMCWLIAF
edg5_human  PVQWFAREGS ASITLSASVF SLLAIAIERH VAIAK.VKLY GSDKSCRMLL LIGASWLISL
edg8_human  PALWFAREGG VFVALTASVL SLLAIALERS LTMAR.RGPA PVSSRGRTLA MAAAAWGVSL
edg6_human  PAQWFLREGL LFTALAASTF SLLFTAGERF ATMVRPVAES GATKTSPVYG FIGLCWLLAA

                181                                                    240
edg2_human  VMGAIPSVGW NCICDIENCS NMAPLYSDSY LVFWAIFNLV TFVVMVVLYA HIFGYVRQRT
edg7_human  FMGAVPTLGW NCLCNISACS SLAPIYSRSY LVFWTVSNLM AFLIMVVVYL RIYVYVKRKT
edg4_human  GLGLLPAHSW HCLCALDRCS RMAPLLSRSY LAVWALSSLL VFLLMVAVYT RIFFYVRRRV
edg1_human  ILGGLPIMGW NCISALSSCS TVLPLYHKHY ILFCTTVFTL LLLSIVILYC RIYSLVRTRS
edg3_human  TLGALPILGW NCLHNLPDCS TILPLYSKKY IAFCISIFTA ILVTIVILYA RIYFLVKSSS
edg5_human  VLGGLPILGW NCLGHLEACS TVLPLYAKHY VLCVVTIFSI ILLAIVALYV RIYCVVRSSH
edg8_human  LLGLLPALGW NCLGRLDACS TVLPLYAKAY VLFCVLAFVG ILAAICALYA RIYCQVRANA
edg6_human  LLGMLPLLGW NCLCAFDRCS SLLPLYSKRY ILFCLVIFAG VLATIMGLYG AIFRLVQASG
```

# FIG. 1C-2

```
                241                                                                  300
edg2_human  MRMSRHSSGP R......RNR DTMMSLLKTV VIVLGAFIIC WTPGLVLLLL D.VCCP..QC
edg7_human  NVLSPHTSGS I......SRR RTPMKLMKTV MTVLGAFVVC WTPGLVVLLL DGLNCR..QC
edg4_human  QRMAEHVSCH P......RYR ETTLSLVKTV VIILGAFVVC WTPGQVVLLL DGLGCE..SC
edg1_human  RRLTFR.... .KNISKASRS SENVALLKTV IIVLSVFIAC WAPLFILLLL DV.GCKVKTC
edg3_human  RKVANH.... .NN......S ERSMALLRTV VIVVSVFIAC WSPLFILFLI DV.ACRVQAC
edg5_human  ADMA..... .........A PQTLALLKTV TIVLGVFIVC WLPAFSILLL DY.ACPVHSC
edg8_human  RRLPARPGTA GTTSTRARRK PRSLALLRTL SVVLLAFVAC WGPLFLLLLL DV.ACPARTC
edg6_human  QKAP...... ...RPAARRK ARR..LLKTV LMILLAFLVC WGPLFGLLLA DVFGSNLWAQ

                301                                                                  360
edg2_human  DVLAYEKFFL LLAEFNSAMN PIIYSYRDKE MSATFRQILC CQRSENPTGP TESSDRSASS
edg7_human  GVQHVKRWFL LLALLNSVVN PIIYSYKDED MYGTMKKMIC CFSQENP... ....ERRPSR
edg4_human  NVLAVEKYFL LLAEANSLVN AAVYSCRDAE MRRTFRRLLC CACLRQSTRE SVHYTSSAQG
edg1_human  DILFRAEYFL VLAVLNSGTN PIIYTLTNKE MRRAFIRIMS CCKCPSGD.. .........S
edg3_human  PILFKAQWFI VLAVLNSAMN PVIYTLASKE MRRAFFRLV. .CNC.LVR.. .........G
edg5_human  PILYKAHYFF AVSTLNSLLN PVIYTWRSRD LRREVLRPLQ CWRPGVGV.. .........Q
edg8_human  PVLLQADPFL GLAMANSLLN PIIYTLTNRD LRHALLRLVC CGRHSCGRDP SGS..QQSAS
edg6_human  EYLRGMDWIL ALAVLNSAVN PIIYSFRSRE VCRAVLSFLC CGCLRLGMRG PGDCLARAVE

                361                                                          418
edg2_human  LNHTILAGVH SNDHSVV--- ---------- ---------- ---------- --------
edg7_human  IPSTVLSRSD TGSQYIEDSI SQGAVCNKST S--------- ---------- --------
edg4_human  GASTRIMLPE NGHPLMTPPF SYLELQRYAA SNKSTAPDDL WVLLAQPNQQ D-------
edg1_human  AGKFKRPIIA GMEFSRSK.. .SDNSSHPQK DEGDNPETIM SSGNVNSSS- --------
edg3_human  RGARASPIQP ALDPSRSKSS SSNNSSHSPK VKEDLPHTDP SSCIMDKNAA LQNGIFCN
edg5_human  GRRRVGTPGH HLLPLRSSSS LERGMHMPTS PTFLEGNTVV ---------- --------
edg8_human  AAEASGGLRR CLPPGLDGSF SGSERSSPQR DGLDTSGSTG SPGAPTAART LVSEPAAD
edg6_human  AHSGASTTDS SLRP.RDSFR GSRSLSFRMR EPLSSISSVR SI-------- --------
```

FIG. 2A

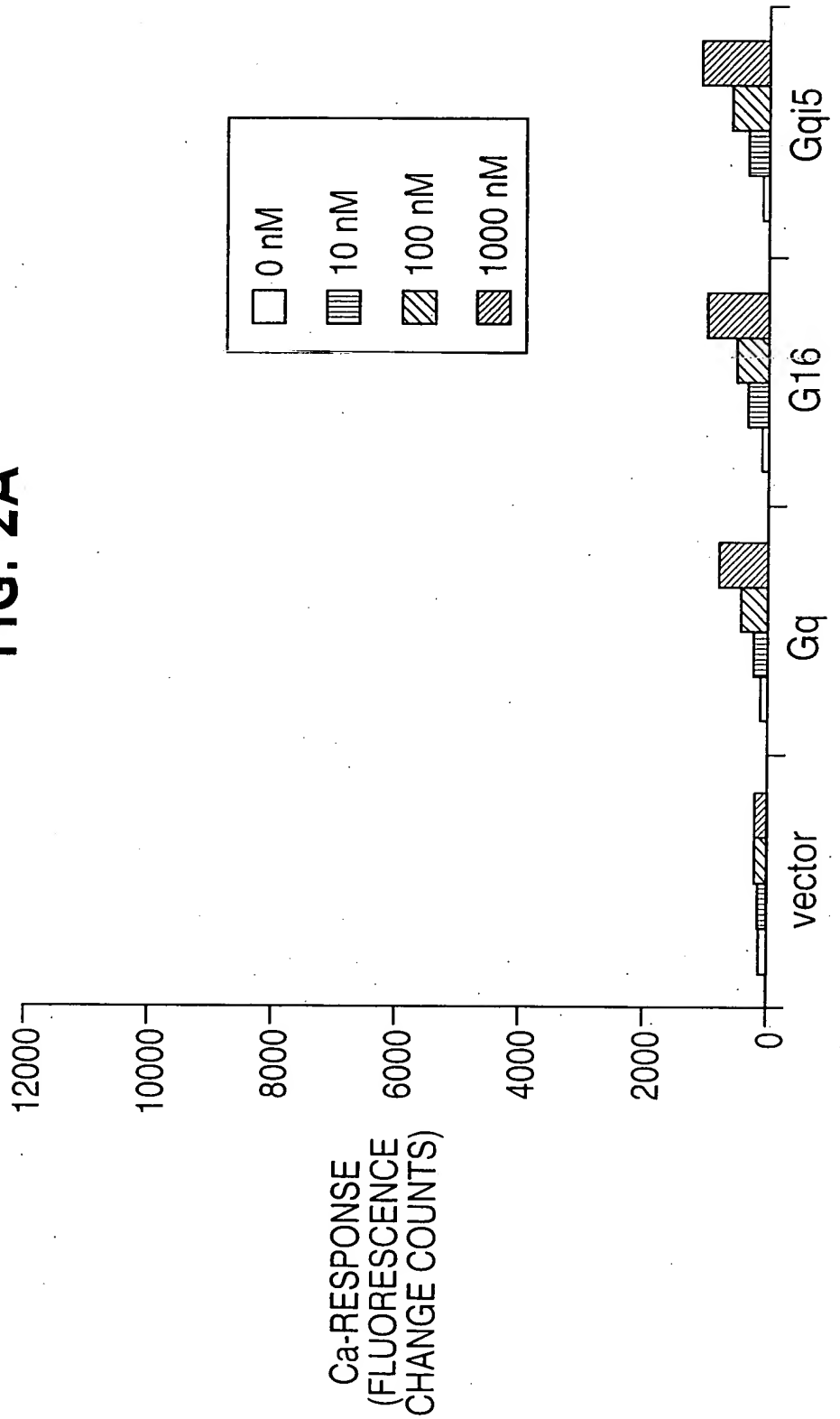


FIG. 2B

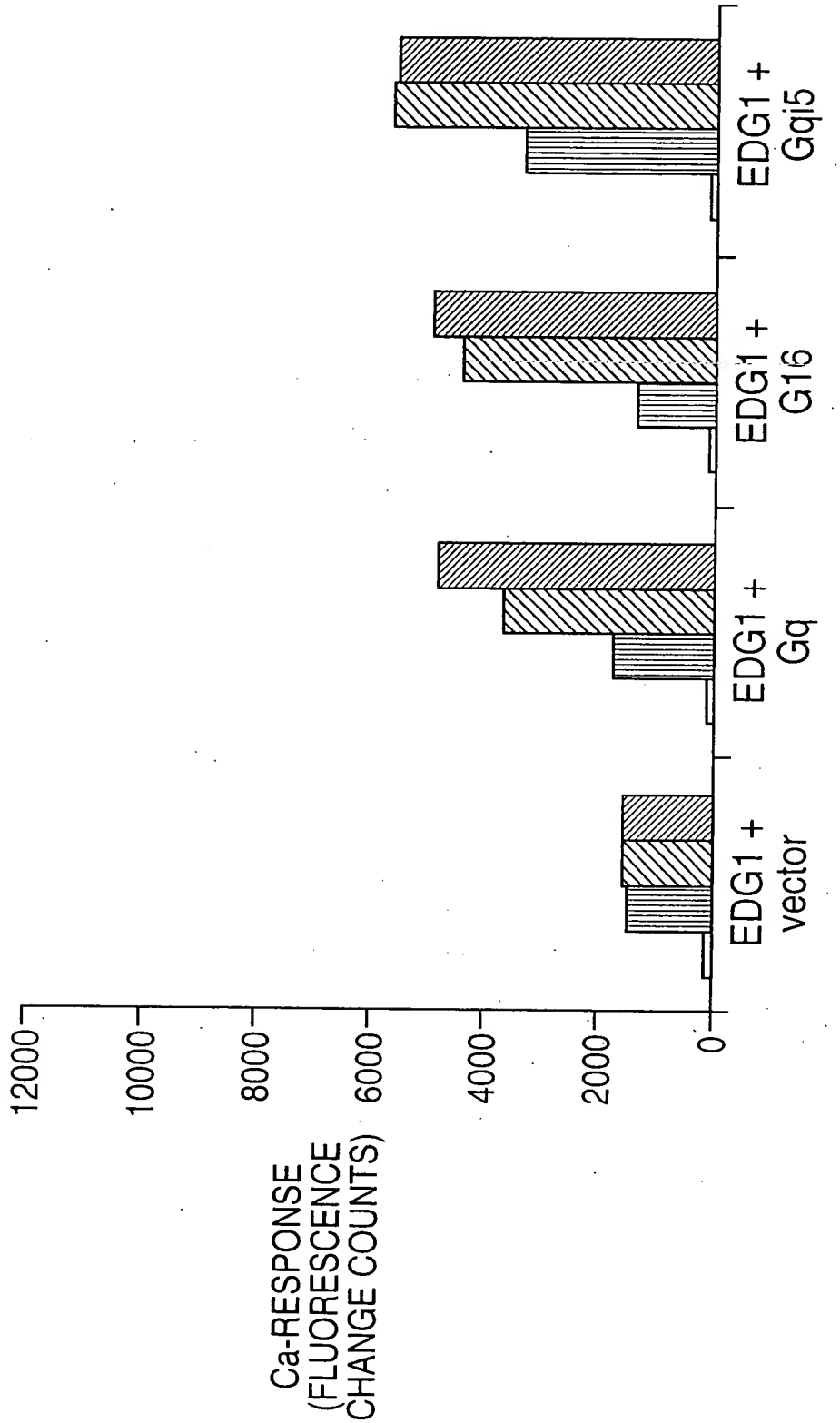


FIG. 2C

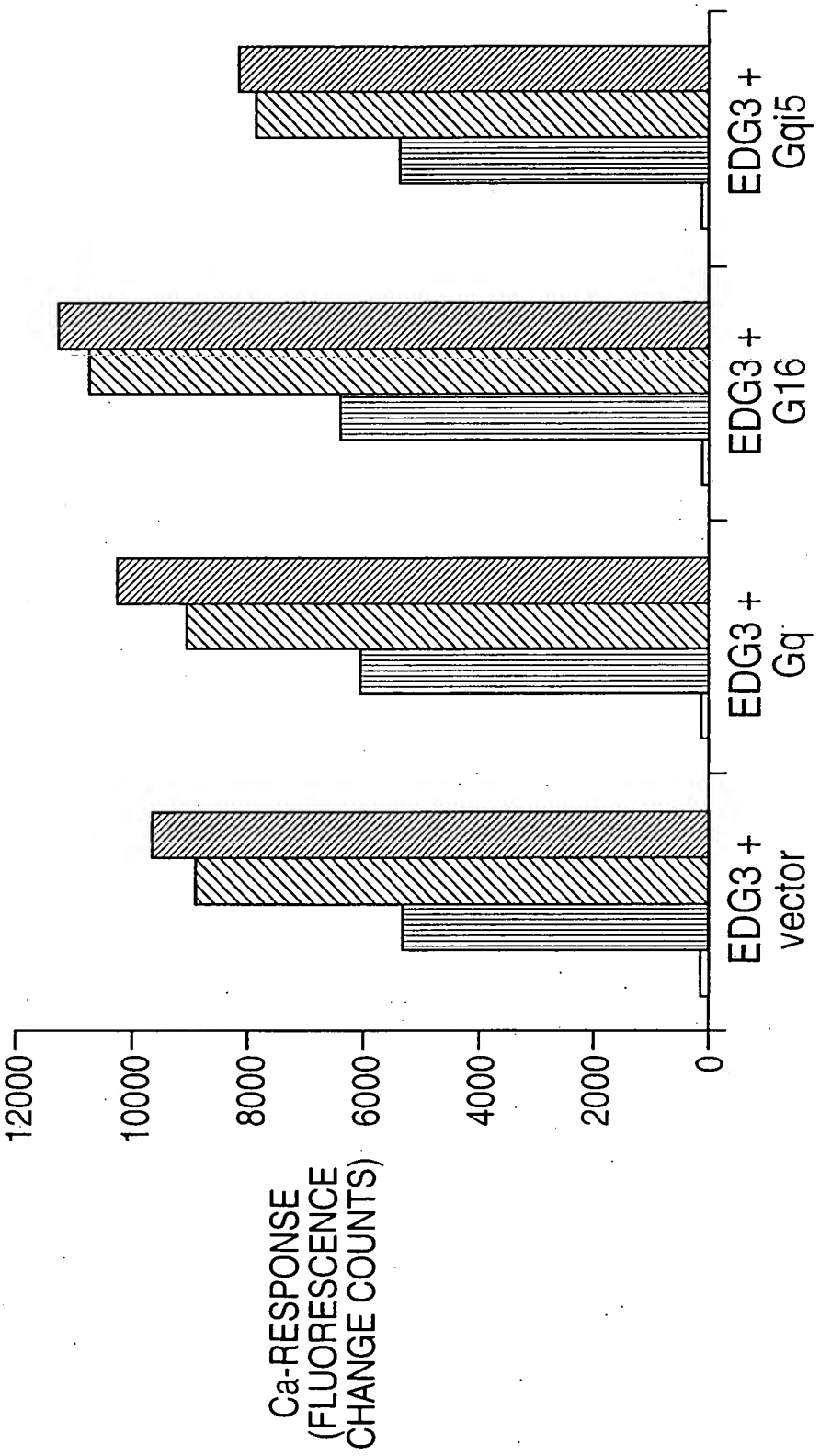


FIG. 2D

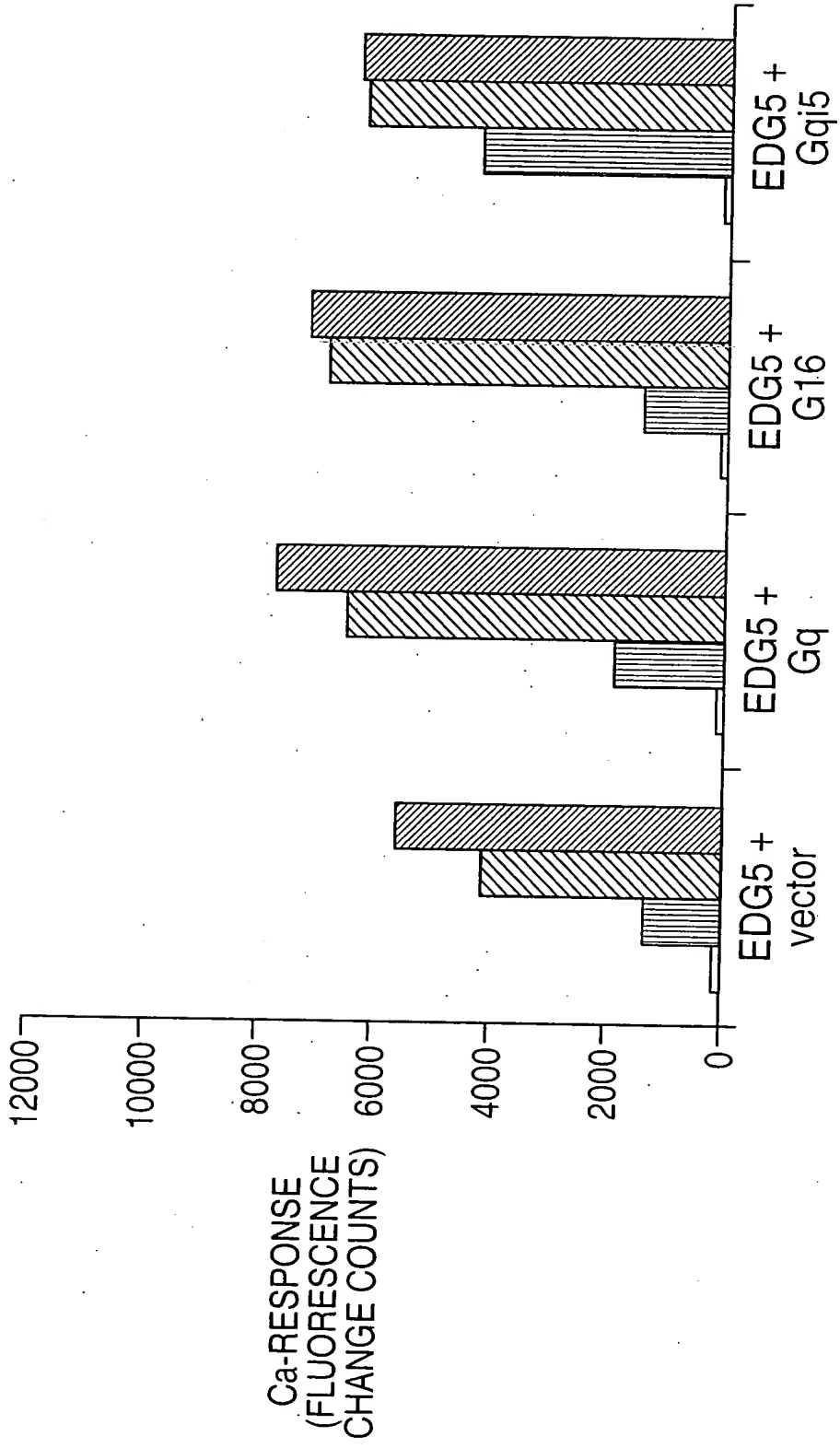


FIG. 2E

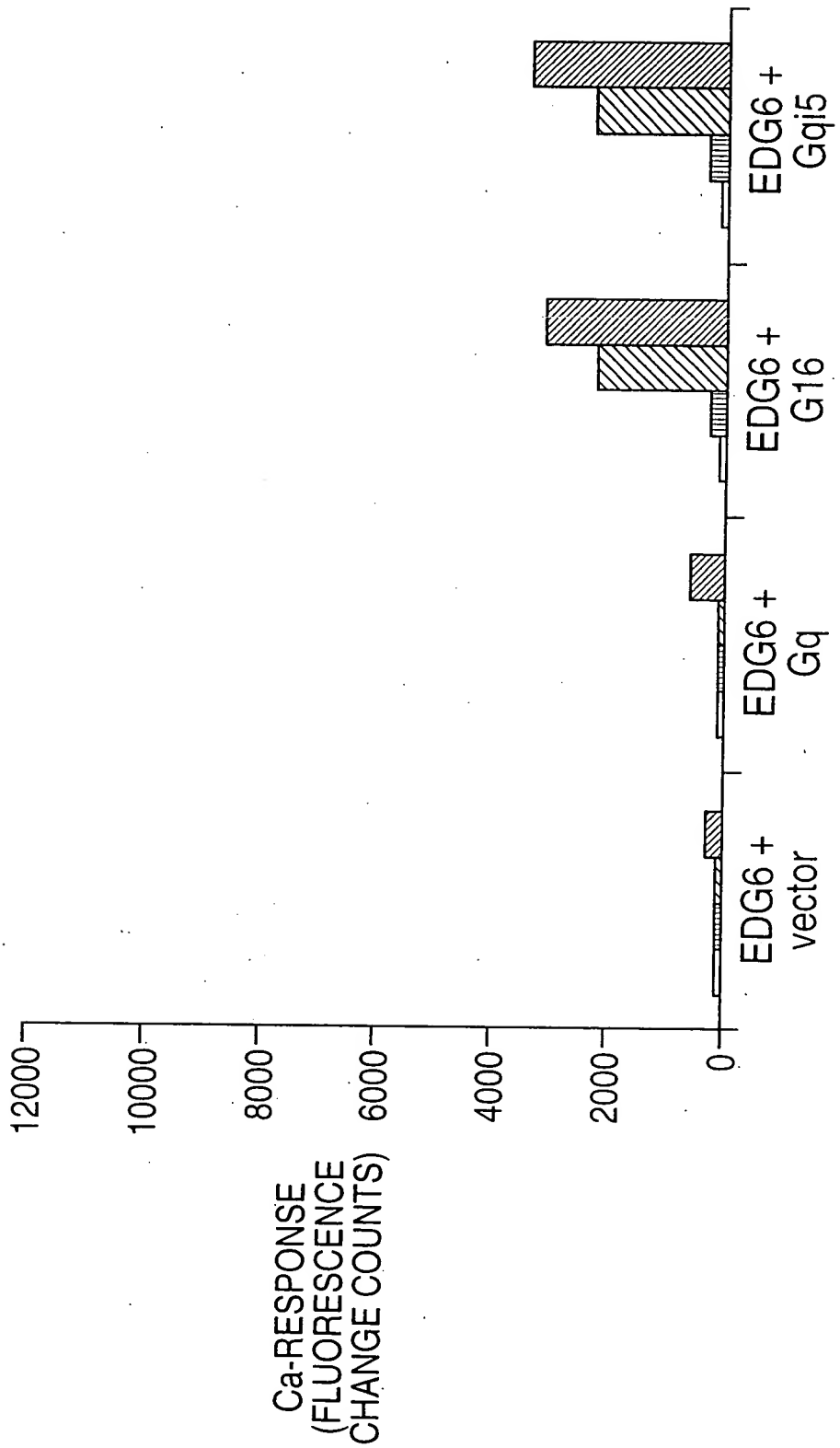


FIG. 2F

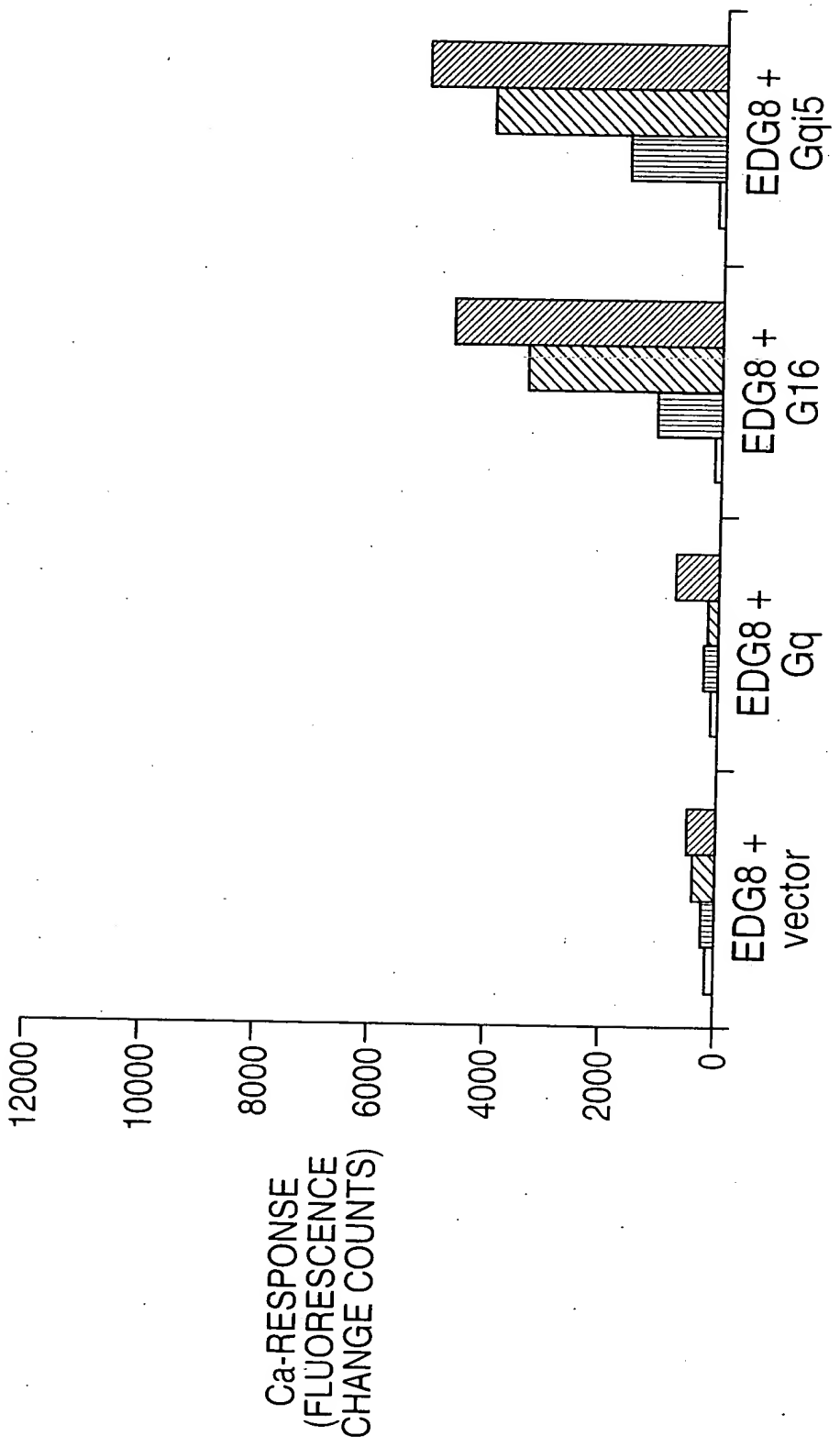


FIG. 3A

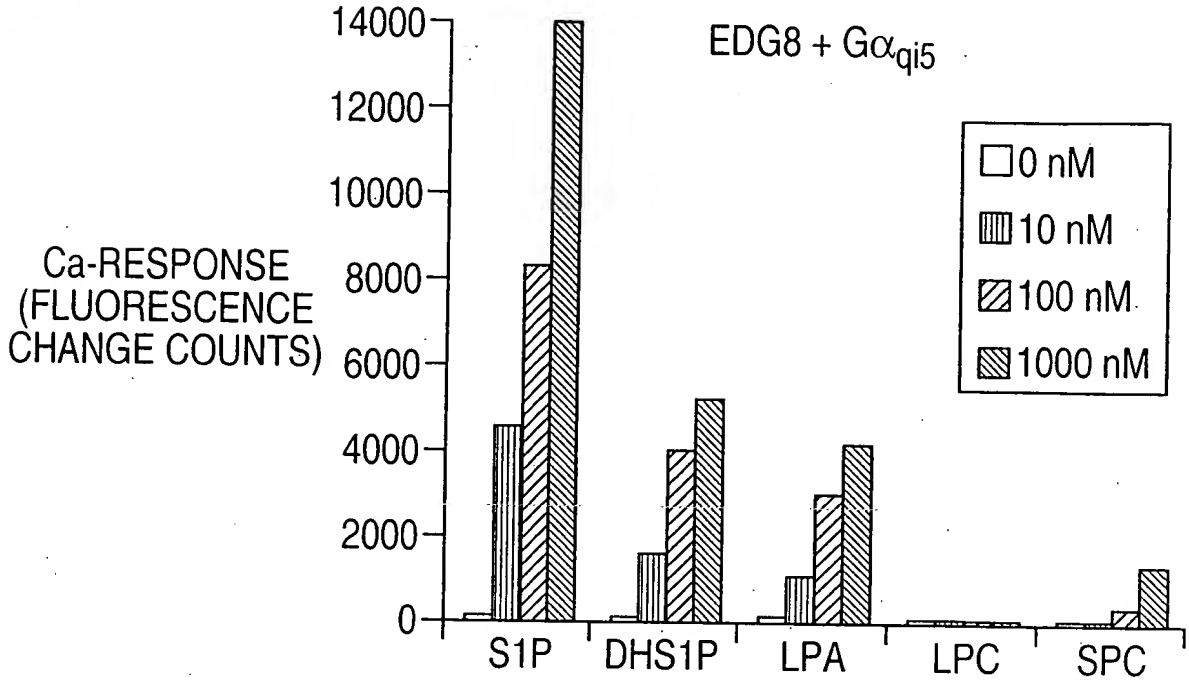



FIG. 3B

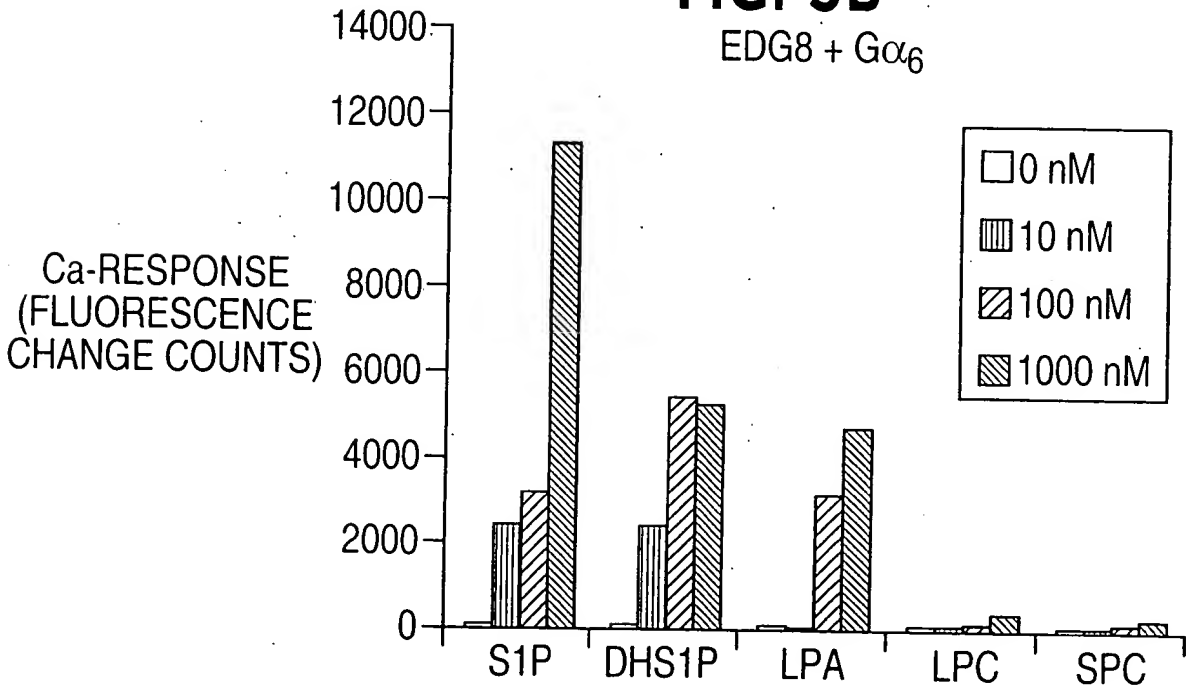


FIG. 4

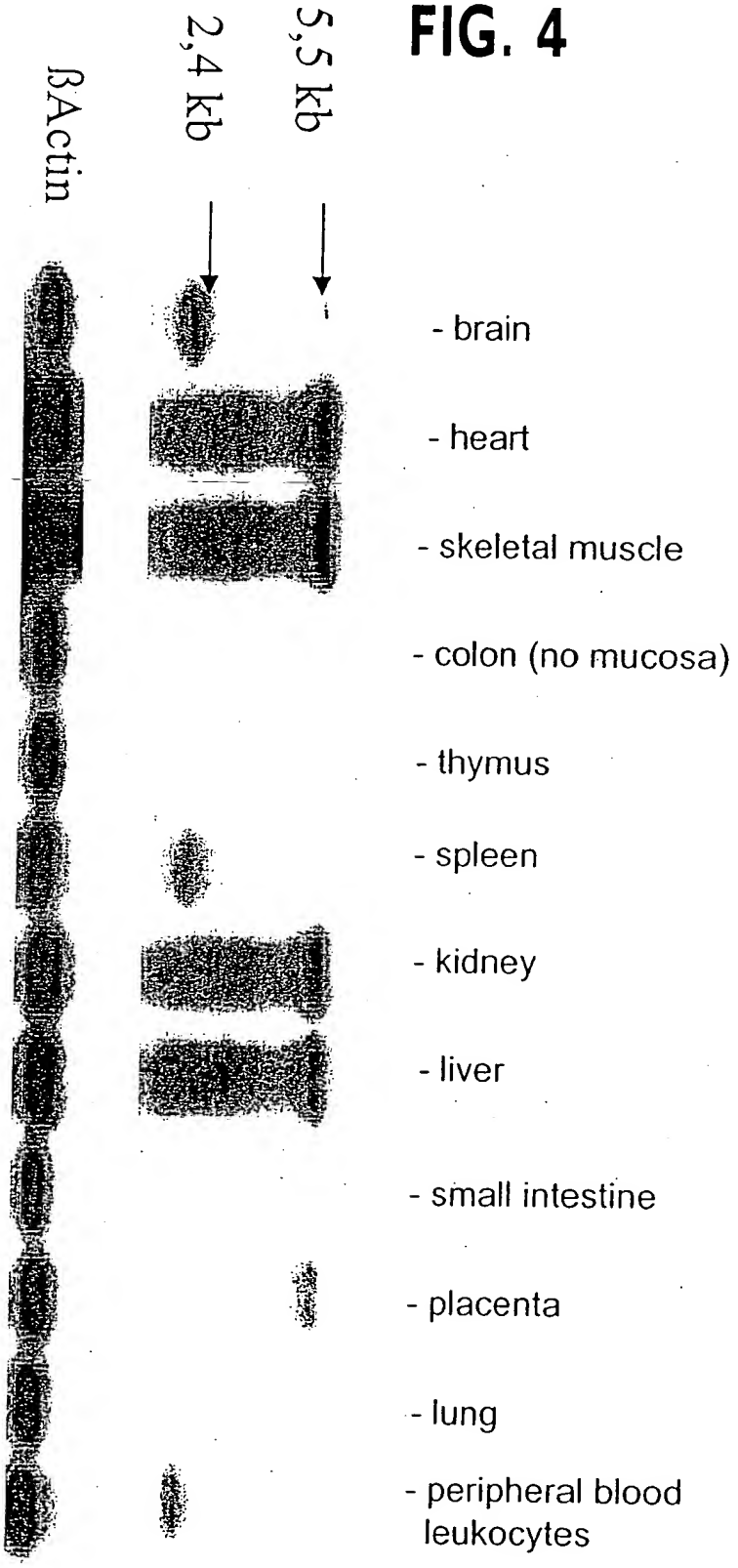


FIG. 5A

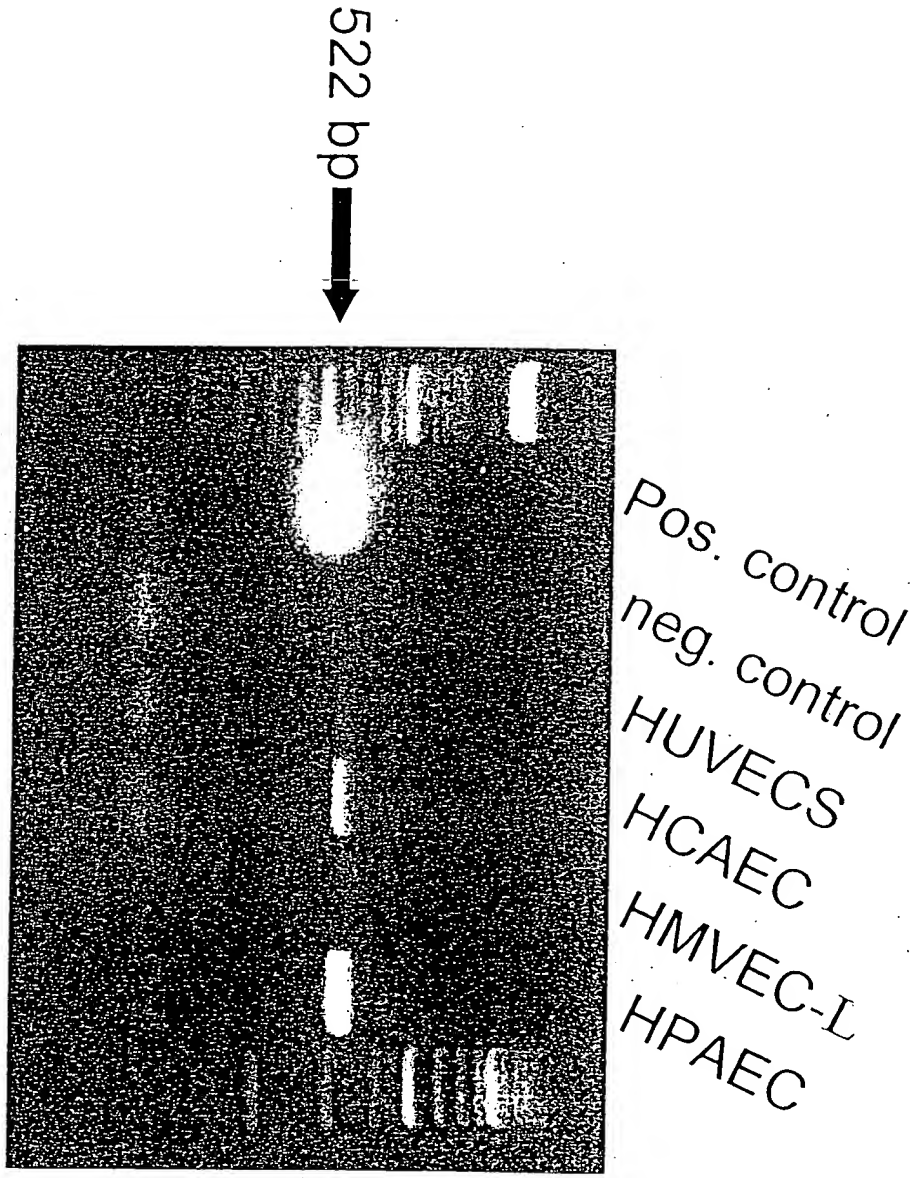
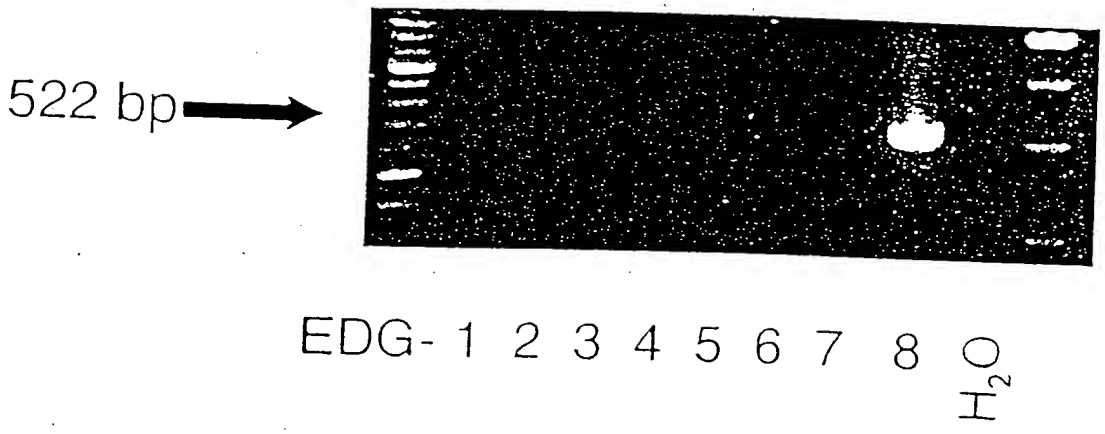
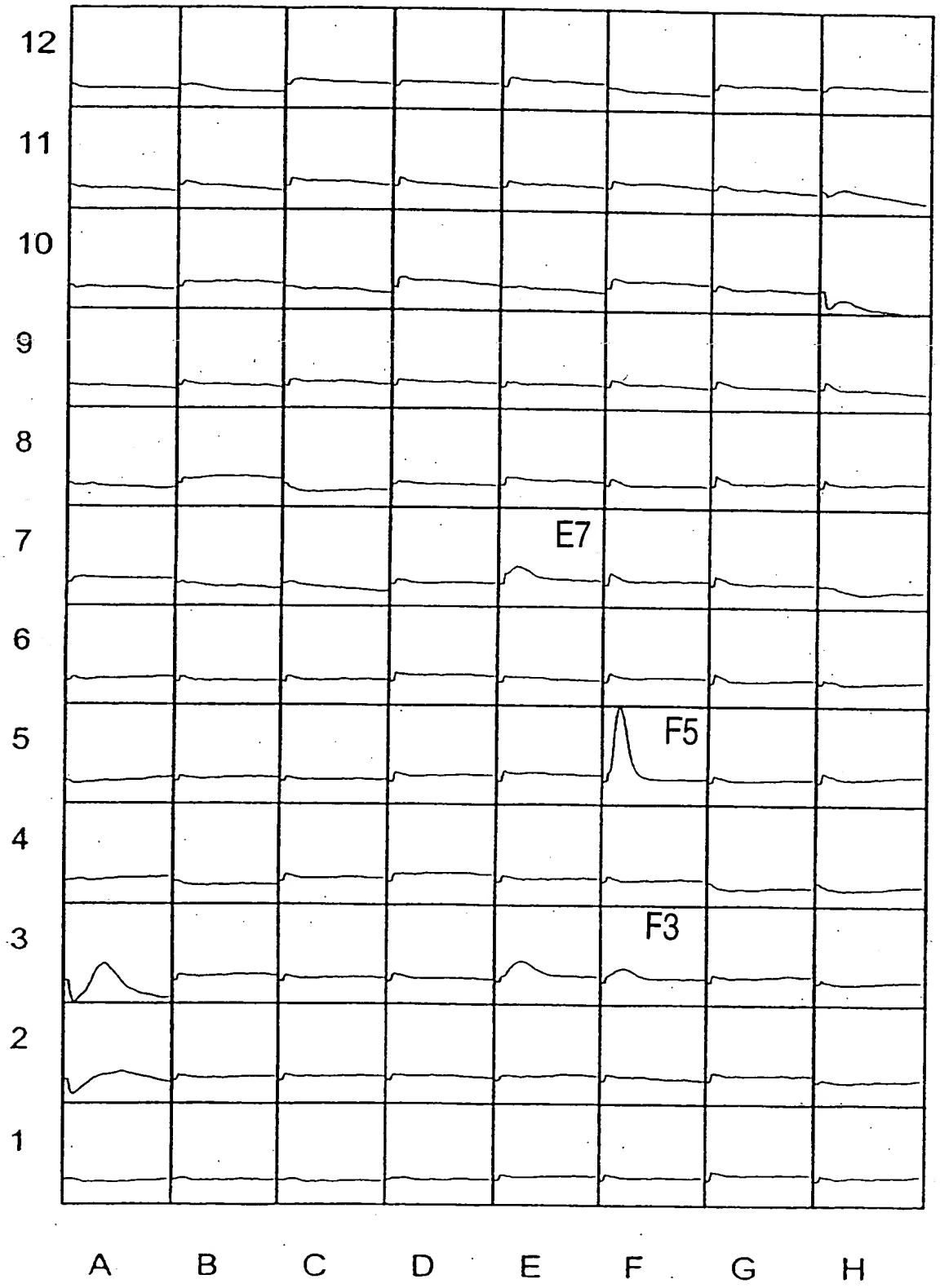


FIG. 5B



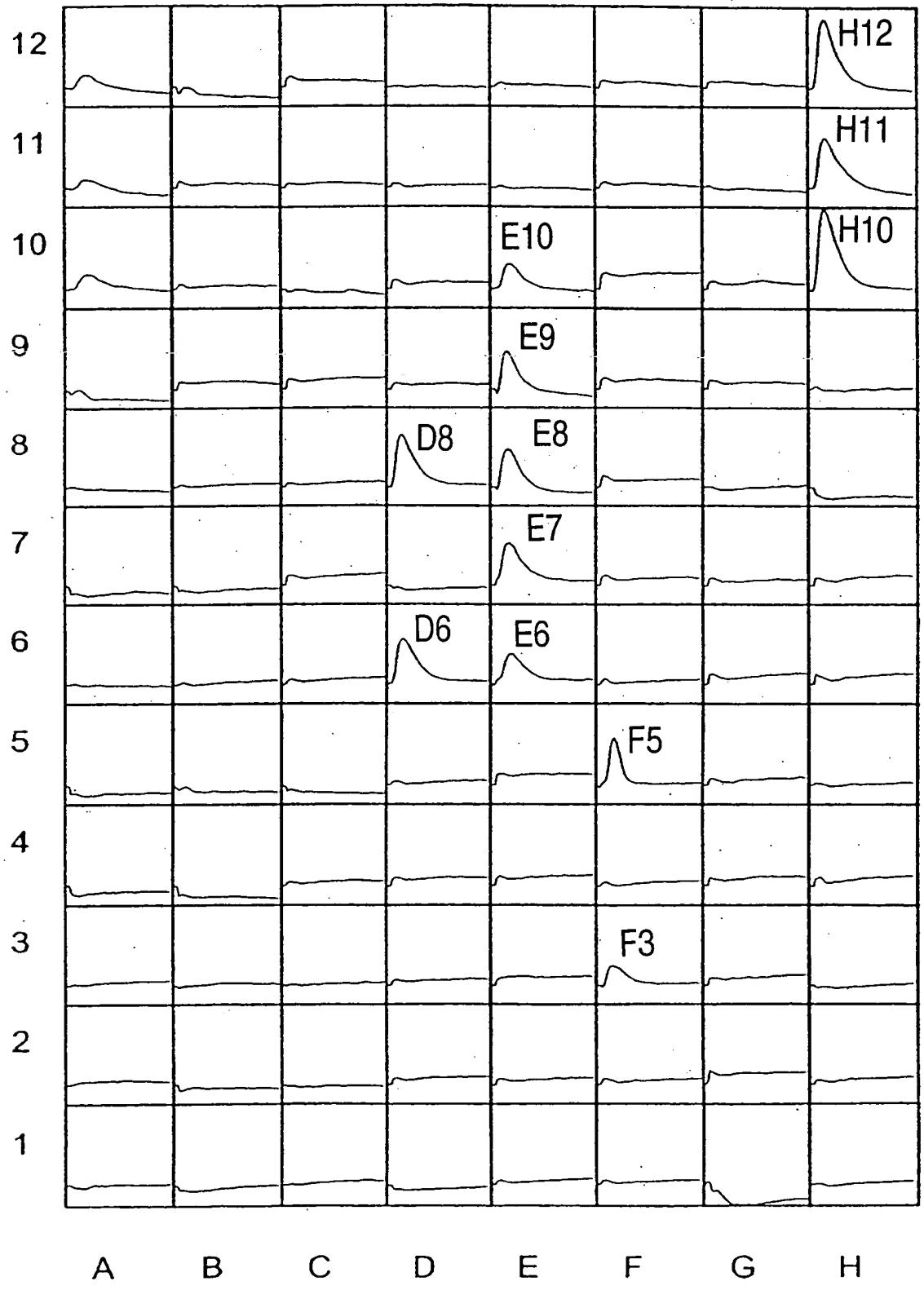
# FIG. 6A

qi5 background



# FIG. 6B

rEDG8



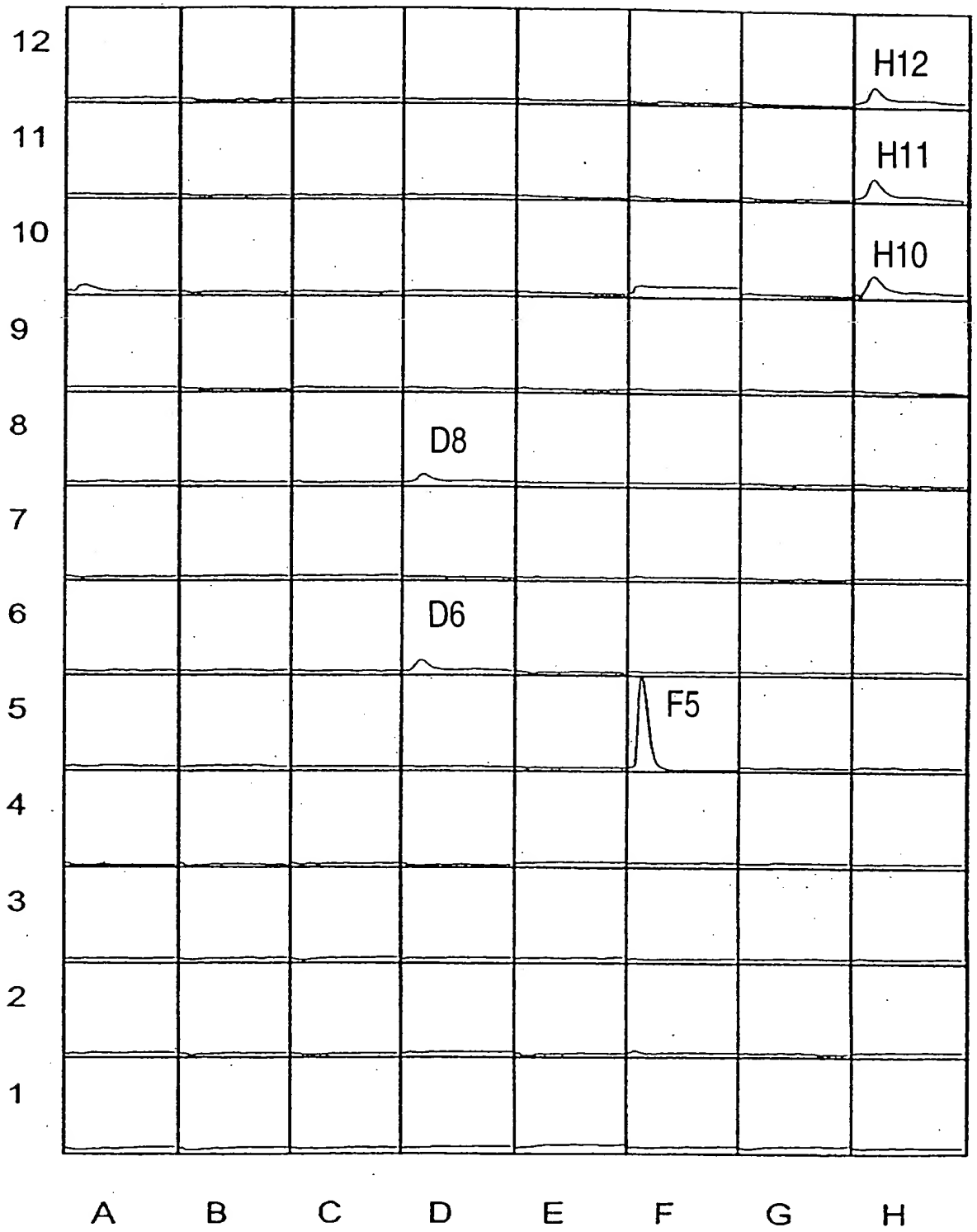
# FIG. 6C

## Fluorescence Change counts

| Wells | Lipid | background | rEDG8 | stand. response |
|---|---|---|---|---|
| H10-H12 | 1μM S1P | 0 | 5196 | 5196 |
| F5 | 1μM LPA | 5893 | 4327 | -1566 |
| F3 | 1μM cPAF | 1017 | 1570 | 553 |
| E10 | 1μM EPA PAF | 0 | 1354 | 1354 |
| E9 | 1μM AA PAF | 0 | 3121 | 3121 |
| E8 | 1μM Enantio PAF | 0 | 3883 | 3883 |
| E7 | 1μM paf C18:1 | 1256 | 3765 | 2509 |
| E6 | 1μM Lyso PAF | 0 | 2421 | 2421 |
| D8 | 1μM dhS1P | 0 | 5144 | 5144 |
| D6 | 1μM S1P | 0 | 3672 | 3672 |

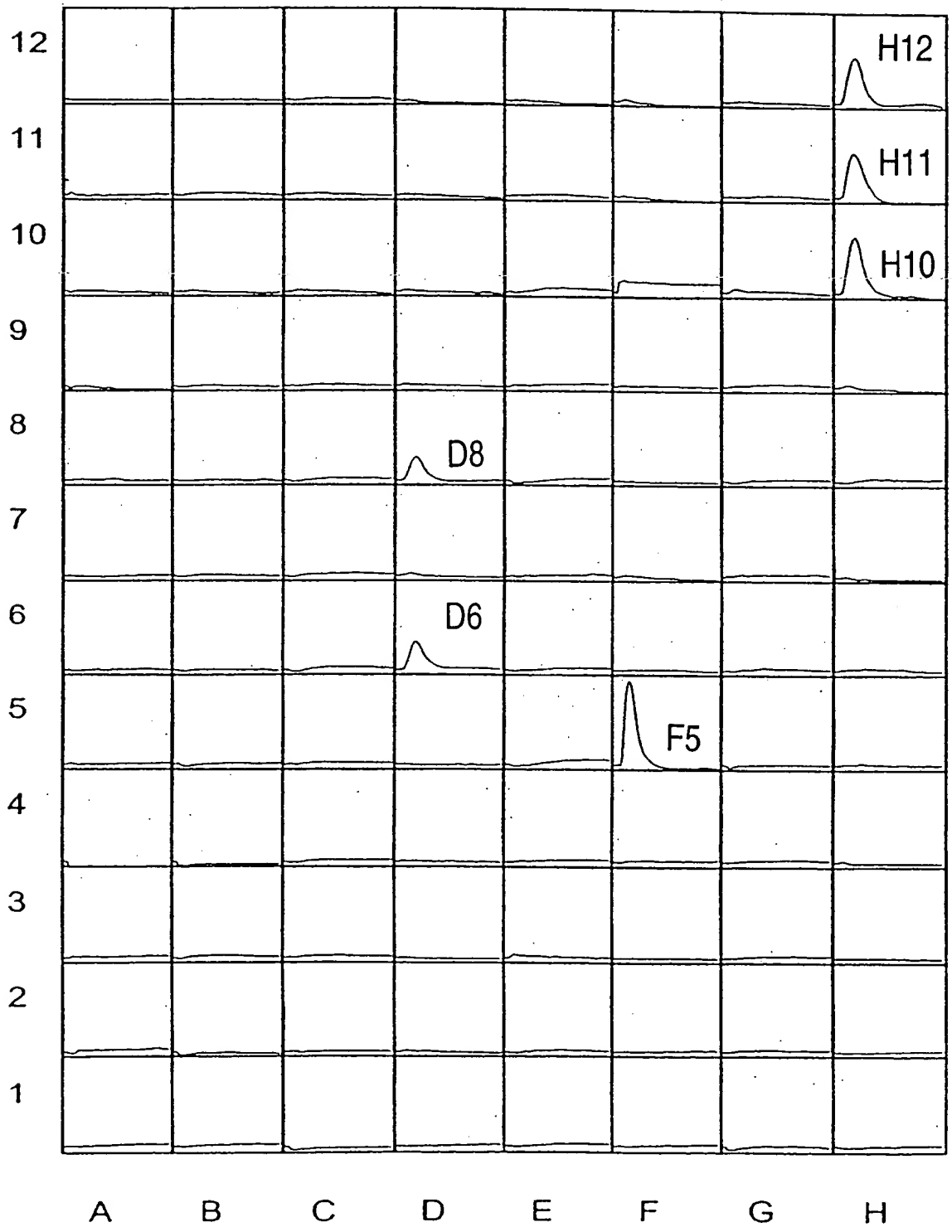
# FIG. 7A

qi5 background in HEK



# FIG. 7B

hEDG8

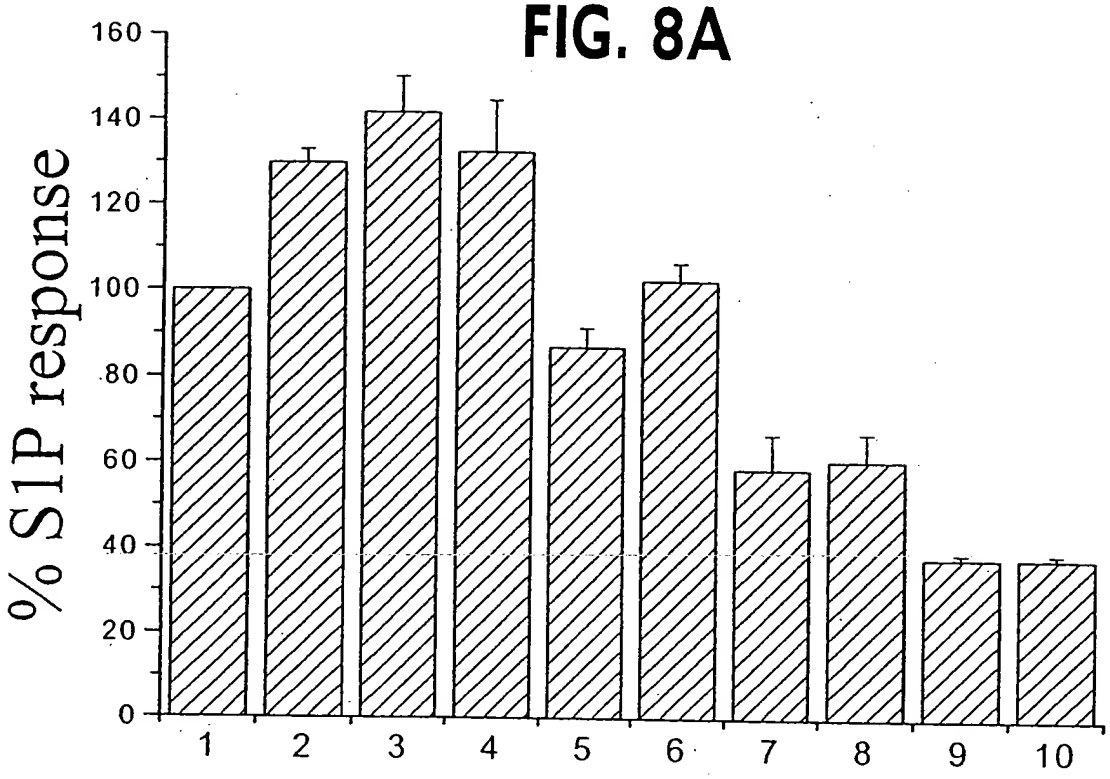


# FIG. 7C

## Fluorescence change counts

| Wells | Lipid | background | hEDG8 | stand. response |
|---|---|---|---|---|
| H10-H12 | 1µM S1P | 3696 | 9493 | 5797 |
| F5 | 1µM LPA | 18004 | 16333 | -1671 |
| D8 | 1µM dhS1P | 1683 | 4522 | 2839 |
| D6 | 1µM S1P | 2273 | 5605 | 3332 |

FIG. 8A




1)S1P 2)Leukotrien B4 3)2 DHLA PAF 4)$C_2$Dihydroceramide
5)15(S)-HEDE 6)PAF C16 7)16,16-Dimethyl $PGE_2$
8)12(R)-HETE 9)8-Epi-$PGF_{2\alpha}$ 10)Leukotoxin A

FIG. 8B

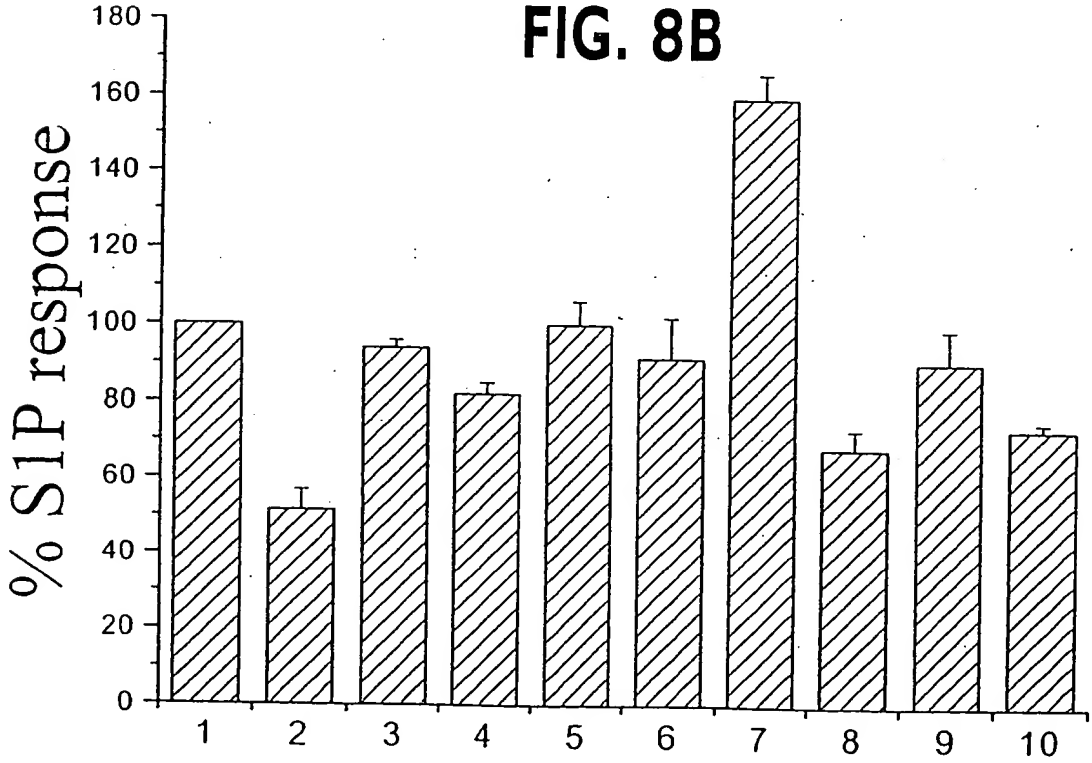


FIG. 9A-1

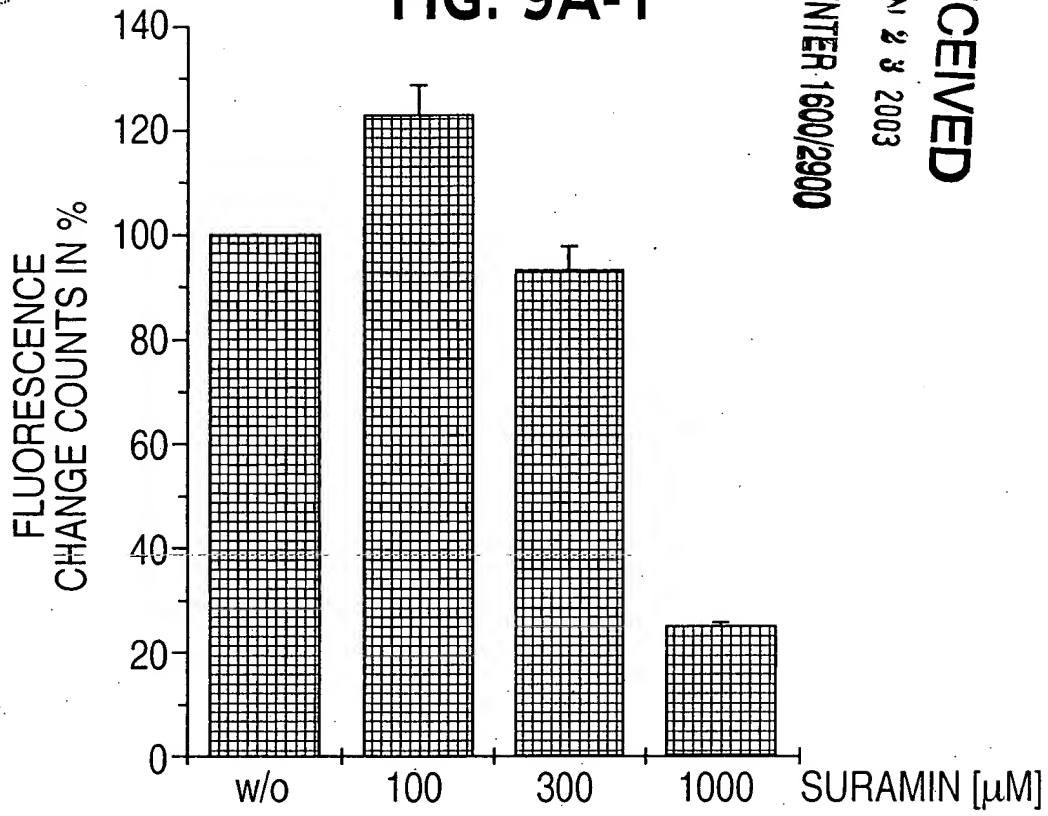



FIG. 9A-2

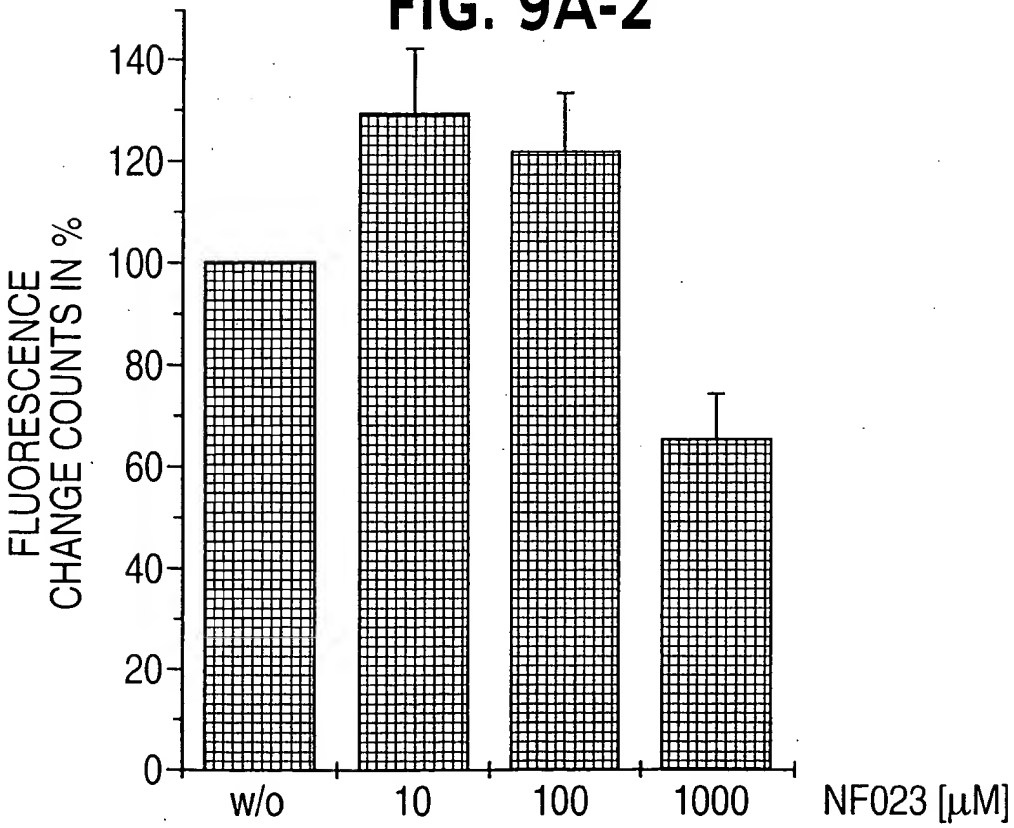


FIG. 9B-1

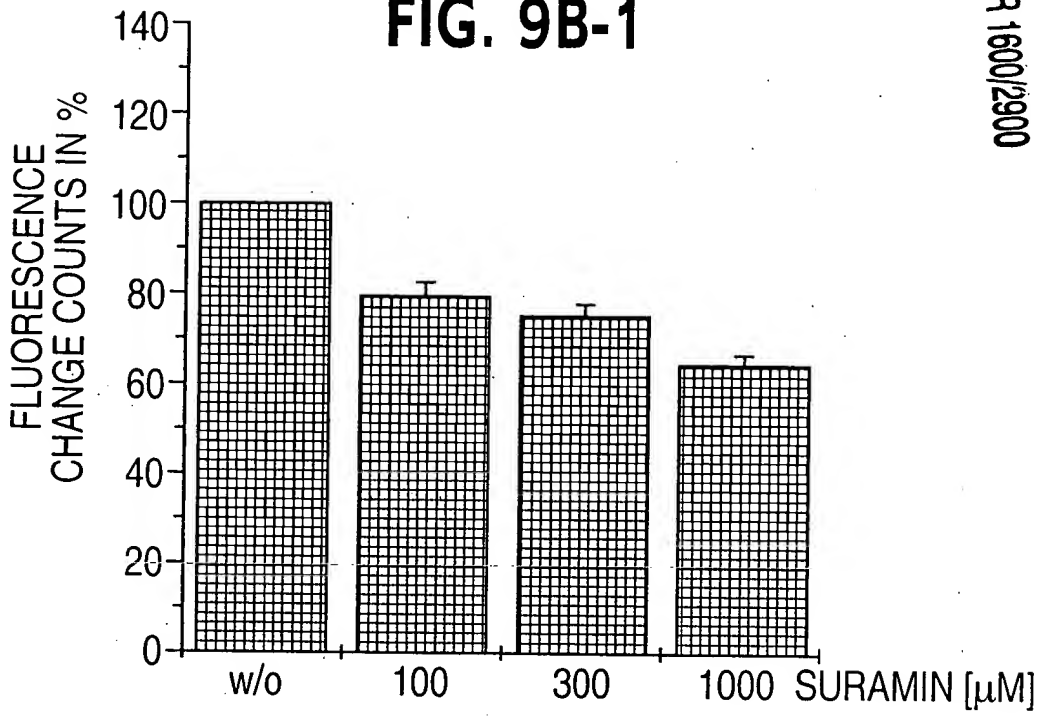



FIG. 9B-2